UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

22/JUL/2008

MEMORANDUM

Subject:	Name of Pesticide Product:	SC 547 Herbicide
	EPA File Symbol:	264-RNAG
	DP Barcode:	D339748
	Decision No.:	378455
	Action Code:	R01.0
	PC Code:	012801 Tembotrione
		015804 Thiencarbazone-methyl

From: Rick J. Whiting, Biologist
Technical Review Branch (TRB)
Registration Division (7505P)

To: Hope Johnson, RM Team 25
Herbicide Branch
Registration Division (7505P)

Applicant: Bayer CropScience
P.O. Box 12014, 2 T.W. Alexander Drive
Research Triangle Park, NC 27709

FORMULATION FROM LABEL:

Active Ingredient(s):		% by wt
015804	Thiencarbazone-methyl (CAS No. 317815-83-1]	5.6
012801	Tembotrione (CAS No. 335104-84-2]	28.3
Inert Ingredient(s):		66.1
	Total:	100.0%

ACTION REQUESTED: The Risk Manager requests: "Bayer CropScience has submitted a new herbicide AI: Thiencarbazone-methyl. This new AI is a Tri-Lateral Review with PMRA and the UK. PMRA may be the lead for the acute toxicology of this end-use product, but it may be EPA. This has not been determined yet. This is a end-use product (264-RNAG) that contains the new AI plus Tembotrione (264-ILO) and a safener. Enclosed are the acute toxicology studies, label and CSF. I've also included the Tembotrione acute toxicology meme. Reviewer will need Circa access for review exchange with UK and PMRA, and must use OECD Tier II template for review."

BACKGROUND: Bayer CropScience has submitted six acute toxicity studies, a Basic Formulation CSF (dated January 17, 2007) and a proposed label to support the registration of SC 547 Herbicide, EPA File Symbol 264-RNAG. The acute toxicity studies were assigned MRID numbers 470703-10 thru -15. The studies were conducted at Eurofins/Product Safety Laboratories. Canada's Pest Management Regulatory Agency (PMRA) conducted the primary review of the studies. TRB performed the secondary review and made changes as necessary.

COMMENTS AND RECOMMENDATIONS:

1. The six studies have been reviewed and classified as Acceptable.

2. The acute toxicity profile for SC 547 Herbicide, EPA File Symbol 264-RNAG, is as follows:

Acute oral toxicity	III	Acceptable	MRID 47070310
Acute dermal toxicity	III	Acceptable	MRID 47070311
Acute inhalation toxicity	IV	Acceptable	MRID 47070312
Primary eye irritation	III	Acceptable	MRID 47070313
Primary skin irritation	IV	Acceptable	MRID 47070314
Dermal sensitization	Negative	Acceptable	MRID 47070315

3. Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System:

PRODUCT ID #: 000264-01063

PRODUCT NAME: SC 547 Herbicide

PRECAUTIONARY STATEMENTS

SIGNAL WORD: CAUTION

Hazards to Humans and Domestic Animals:

Harmful if absorbed through skin. Harmful if swallowed. Causes moderate eye irritation. [Wear protective eyewear.]* Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Wear long-sleeved shirt and long pants, socks, shoes, and chemical-resistant gloves (such as Natural Rubber, Selection Category A). Remove and wash contaminated clothing before reuse.

*[Protective eyewear may be specified, if appropriate]

First Aid:

If on skin: Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.

If swallowed: Call a poison control center or doctor immediately for treatment advice. Have person sip a glass of water if able to swallow. Do not induce vomiting unless told to by a poison control center or doctor. Do not give anything to an unconscious person.

If in eyes: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

4. The Basic Formulation CSF (dated January 17, 2007) for the proposed product should also be reviewed and accepted by the TRB Chemistry Team.

Reviewer: PMRA
Risk Manager (EPA): 25

Date: July 22, 2008

STUDY TYPE: Acute Oral Toxicity - Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid]

CITATION: Durando, J. (2007) SP102000016695 (636+747+(Inert Ingredient) SC): Acute Oral Toxicity Up and Down Procedure in Rats: (SC 547 Herbicide). Project Number: 21163, P320/UDP, M-284724-01-1. Unpublished study prepared by Product Safety Laboratories. 15 p. February 8, 2007. MRID No. 47070310

SPONSOR: Bayer CropScience, 2 T.W. Alexander Drive, P.O. Box 12014, Research Triangle Park, NC 27709

EXECUTIVE SUMMARY: An acute oral toxicity test (Up and Down Procedure; MRID 47070310) was conducted with rats to determine the potential for SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid) to produce toxicity from a single dose via the oral route. Under the conditions of this study, the acute oral LD_{50} of the test substance is greater than 2,000 mg/kg of body weight in female rats. Based on the results of this study, SP102000016695 meets the requirements for EPA Toxicity Category III for oral toxicity.

An initial limit dose of 2,000 mg/kg was administered to one healthy female rat by oral gavage. Due to the absence of mortality in this animal, four additional female rats received the same dose level sequentially. Since these animals survived, no additional animals were tested. Females were selected for the test because they are frequently more sensitive to the toxicity of test compounds than males. All animals were observed for mortality, signs of gross toxicity, and behavioral changes at least once daily for 14 days after dosing. Body weights were recorded prior to administration and again on Days 7 and 14 (termination) following dosing. Necropsies were performed on all animals at terminal sacrifice.

All animals survived, gained body weight, and appeared active and healthy during the study. There were no signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. **Test Material:** SP102000016695
   Description: Light tan opaque liquid
   Lot # 06DAL005P113
   Purity: Thiencarbazone-methyl: 5.81%
   Tembotrione): 29.03%
   CAS #: 317815-83-1; 335104-84-2

2. **Vehicle and/or positive control:** None

3. **Test animals:**

Species:	Rat	
Strain:	Sprague-Dawley derived, albino	
Age/weight at dosing:	10-11 weeks	
Source:	Ace Animals, Inc., Boyertown, PA	
Housing:	Singly housed in suspended stainless steel caging with mesh floors	
Diet:	Purina Rodent Chow, PMI #5012 *ad libitum*	
Water:	Filtered tap water *ad libitum*	
Environmental conditions:	**Temperature:**	19-23°C
	Humidity:	30-69%RH
	Air changes:	10/hr
	Photoperiod:	12 hrs dark/12 hrs light
Acclimation period:	13-22 days	

B. STUDY DESIGN and METHODS:

1. **In life dates** - Start: November 22, 2006 End: December 18, 2006

2. **Animal assignment and treatment** - Animals were assigned to the test groups noted in Table 1. Following an overnight fast, rats were given a single dose of SP102000016695 by gavage then observed (first several hours post-dosing and at least once daily thereafter for 14 days) and weighed prior to test substance administration (initial) and again on Days 7 and 14 (termination). All animals were sacrificed and a necropsy was performed.

3. Statistics - The *Acute Oral Toxicity (Guideline 425) Statistical Program* (Weststat, version 1.0, May 2001) was used for all data analyses including: dose progression selections, stopping criteria determinations and/or LD_{50} and confidence limit calculations.

II. RESULTS AND DISCUSSION:

A. Mortality is given below in Table 1. The acute oral LD_{50} of SP102000016695 (636+747+Isoxadifen SC) is greater than 2,000 mg/kg in female rats.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg bw)	Females	Mortality (day of test)
2,000	0/5	N/A

B. Clinical observations – Following administration, all animals survived and appeared active and healthy during the study. There were no signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior.

C. Body Weight - All animals gained body weight over the 14-day observation period.

D. Necropsy – No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

E. Applicant's Conclusions: The acute oral LD_{50} of SP102000016695 is greater than 2,000 milligrams per kilogram of body weight in female rats. Based on the results of this study, SP102000016695 meets the requirements for EPA Toxicity Category III for oral toxicity.

Reviewer: PMRA
Risk Manager (EPA): 25
Date: July 22, 2008

STUDY TYPE: Acute Dermal Toxicity - Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid]

CITATION: Durando, J. (2007) SP102000016695 (636+747+(Inert Ingredient) SC): Acute Dermal Toxicity Study in Rats - Limit Test: (SC 547 Herbicide). Project Number: 21164, P322/RAT, M-284725-01-1. Unpublished study prepared by Product Safety Laboratories. 15 p. February 8, 2007. MRID No. 47070311

SPONSOR: Bayer CropScience, 2 T.W. Alexander Drive, P.O. Box 12014, Research Triangle Park, NC 27709

EXECUTIVE SUMMARY: An acute dermal toxicity test (MRID 47070311) was conducted with rats to determine the potential for SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid] to produce toxicity from a single topical application. Under the conditions of this study, the single dose acute dermal LD_{50} of the test substance is greater than 2,000 mg/kg of body weight in male and female rats. Based on the results of this study, SP102000016695 meets the requirements for EPA Toxicity Category III for dermal toxicity.

Two thousand milligrams of the test substance per kilogram of body weight was applied to the skin of ten healthy rats for 24 hours. The animals were observed for mortality, signs of gross toxicity, and behavioral changes at least once daily for 14 days. Body weights were recorded prior to application and again on Days 7 and 14 (termination). Necropsies were performed on all animals at terminal sacrifice.

All animals survived, gained body weight, and appeared active and healthy during the study. There were no signs of gross toxicity, dermal irritation, adverse pharmacologic effects, or abnormal behavior. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. **Test Material:** SP102000016695
   Description: Light tan opaque liquid
   Lot # 06DAL005P113
   Purity: Thiencarbazone-methyl: 5.81%
   Tembotrione): 29.03%
   CAS #: 317815-83-1; 335104-84-2

2. **Vehicle and/or positive control: None**

3. **Test animals:**

Species:	Rat	
Strain:	Sprague-Dawley derived, albino	
Age/weight at dosing:	10-11 weeks	
Source:	Ace Animals, Inc., Boyertown, PA	
Housing:	Singly housed in suspended stainless steel caging with mesh floors	
Diet:	Purina Rodent Chow, PMI #5012 *ad libitum*	
Water:	Filtered tap water *ad libitum*	
Environmental conditions:	**Temperature:**	19-24°C
	Humidity:	30-70%RH
	Air changes:	15/hr
	Photoperiod:	12 hrs dark/12 hrs light
Acclimation period:	21 days	

B. STUDY DESIGN and METHODS:

1. **In life dates** - Start: November 28, 2006 End: December 12, 2006

2. **Animal assignment and treatment** - Animals were assigned to the test groups noted in Table 1. On the day prior to application, a group of animals was prepared by clipping (Oster model #A5-small) the dorsal area and the trunk. Animals were given a single dermal dose of SP102000016695, applied to a dose area of approximately 2 inches x 3 inches (approximately 10% of the body surface) and covered with a 2-inch x 3-inch, 4-ply gauze pad. The gauze pad and entire trunk of each animal were then wrapped with 3-inch Durapore tape to avoid dislocation of the pad and to minimize loss of the test substance. After 24 hours of exposure to the test substance, the pads were removed and the test sites were gently cleansed of any residual test substance with 1% soap solution and tap water and a clean paper towel. All animals were observed during the first several hours after application and at least once daily thereafter for 14

days and weighed prior to test substance application (initial) and again on Days 7 and 14 (termination). All animals were sacrificed and a necropsy was performed.

3. Statistics - Not applicable.

II. RESULTS AND DISCUSSION:

A. Mortality is given in Table 1. The acute dermal LD_{50} for males and females is greater than 2,000 mg/kg bw.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg bw)	Males	Females	Combined
2,000	0/5	0/5	0/10

B. Clinical observations - All animals appeared active and healthy during the study. There were no signs of gross toxicity, dermal irritation, adverse clinical signs, or abnormal behavior.

C. Body Weight - All animals gained body weight during the study.

D. Necropsy - No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

E. Applicant's Conclusions: The dermal LD_{50} of the test substance for males and females is greater than 2,000 mg/kg bw. Based on the results of this study, SP102000016695 meets the requirements for EPA Toxicity Category III for dermal toxicity.

Reviewer: PMRA
Risk Manager (EPA): 25

Date: July 22, 2008

STUDY TYPE: Acute Inhalation Toxicity - Rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid]

CITATION: Durando, J. (2007) SP102000016695 (636+747+(Inert Ingredient) SC): Acute Inhalation Toxicity Study in Rats - Limit Test: (SC 547 Herbicide). Project Number: 21165, P330, M-284727-01-1. Unpublished study prepared by Product Safety Laboratories. 22 p. February 8, 2007. MRID No. 47070312

SPONSOR: Bayer CropScience, 2 T.W. Alexander Drive, P.O. Box 12014, Research Triangle Park, NC 27709

EXECUTIVE SUMMARY: An acute inhalation toxicity test (MRID 47070312) was conducted with rats to determine the potential for SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid] to produce toxicity from a single exposure via the inhalation (nose-only exposure) route. Under the conditions of this study, the single exposure acute inhalation LC_{50} of the test substance is greater than 2.04 mg/L in male and female rats. Based on the results of this study, SP102000016695 meets the requirements for EPA Toxicity Category IV for inhalation toxicity.

After establishing the desired generation procedures during pre-test trials, ten healthy rats (5/sex) were exposed to the test atmosphere for 4 hours. Chamber concentration and particle size distributions of the test substance were determined periodically during the exposure period. The animals were observed for mortality, signs of gross toxicity, and behavioral changes at least once daily for 14 days following exposure. Body weights were recorded prior to exposure and again on Days 7 and 14 (termination). Necropsies were performed on all animals at terminal sacrifice.

All animals survived exposure to the test atmosphere and gained body weight over the 14-day observation period. The gravimetric chamber concentration was 2.04 mg/L. Based on graphic analysis of the particle size distribution as measured with an Andersen Cascade Impactor, the mass median aerodynamic diameter was estimated to be 3.45 μm.

Over the entire 14-day observation period following exposure, all animals appeared active and healthy. There were no signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. **Test Material:** SP102000016695
   Description: Light tan opaque liquid
   Lot # 06DAL005P113
   Purity: Thiencarbazone-methyl: 5.81%
   Tembotrione): 29.03%
   CAS #: 317815-83-1; 335104-84-2

2. **Vehicle and/or positive control:** None

3. **Test animals:**

Species:	Rat	
Strain:	Sprague-Dawley derived, albino	
Age/weight at dosing:	9-10 weeks	
Source:	Ace Animals, Inc., Boyertown, PA	
Housing:	Singly housed in suspended stainless steel caging with mesh floors	
Diet:	Purina Certified Rodent Diet, PMI #5002 *ad libitum*	
Water:	Filtered tap water *ad libitum*	
Environmental conditions:	**Temperature:**	19-22°C
	Humidity:	36-66%RH
	Air changes:	13/hr
	Photoperiod:	12 hrs dark/12 hrs light
Acclimation period:	14 days	

B. STUDY DESIGN and METHODS:

1. **In life dates** - Start: November 28, 2006 End: December 12, 2006

2. **Exposure conditions**

3. **Animal assignment and treatment** - Animals were assigned to the test groups noted in Table 1 below. Ten healthy rats (five males and five females) were selected for test. The animals were acclimated to the nose-only inhalation chamber for a minimum of 30 minutes prior to exposure and re-examined for health just prior to exposure. Animals were exposed to the test atmosphere for four hours then removed to individual cages for observation. All animals were observed for mortality during the exposure period. The animals were examined for signs of gross toxicity, and behavioral changes upon removal from the exposure tube and at least once daily thereafter for 14 days. Individual body weights of the animals were recorded prior to test substance

exposure (initial) and again on Days 7 and 14 (termination). All rats were euthanized via CO_2 inhalation at the end of the 14-day observation period. Gross necropsies were performed on all animals. Tissues and organs of the thoracic and abdominal cavities were examined.

4. Generation of the test atmosphere / chamber description: The times for 90 and 99% equilibration of the chamber atmosphere were 0.5 and 1.0 minutes, respectively.

Atmosphere Generation: The test atmosphere was generated using a ¼ inch JCO atomizer, (Spraying Systems Co.), FC3 fluid cap (Robert Miller Associates) and 70 SS (Spraying Systems Co.). Compressed air was supplied at 30 psi. The test substance was metered to the atomization nozzle through size 16 tygon tubing (Master Flex), using a peristaltic pump (Master Flex, Model #7520-35). During exposure, the test mixture was kept on a magnetic stir plate.

Test atmosphere concentration: Gravimetric samples were withdrawn at 6 intervals from the breathing zone of the animals. Samples were collected using 25 mm glass fiber filters (GF/B Whatman) in a filter holder attached by ¼ inch tygon tubing to a vacuum pump (Reliance Electric, Model #G557X). Filter papers were weighed before and after collection to determine the mass collected. This value was divided by the total volume of air sampled to determine the chamber concentration. The collections were carried out for 3 minutes at airflows of 4 Lpm. Sample airflows were measured using a Mass Flowmeter (Omega, Model #FMA 5610). Results as gravimetric concentration are in Table 1 below.

Particle size determination: An eight-stage Andersen cascade impactor was used to assess the particle size distribution of the test atmosphere. Samples were withdrawn from the breathing zone of the animals at two intervals. The filter paper collection stages were weighed before and after sampling to determine the mass collected upon each stage. The aerodynamic mass median diameter and geometric standard deviation were determined graphically using two-cycle logarithmic probit axes. Results are reported as MMAD in Table 1 below.

5. Statistics – Not applicable

II. RESULTS AND DISCUSSION:

A. Mortality is given in Table 1. The acute inhalation LC_{50} for males and females is greater than 2.04 mg/L.

TABLE 1. Concentrations, exposure conditions, mortality/animals treated

Nominal Conc. (mg/L)	Gravimetric Conc. (mg/L)	MMAD µm	GSD	Mortality (# dead/total)		
				Males	Females	Combined
692.49	2.04	3.45	1.96	0/5	0/5	0/10

B. Clinical observations - Over the entire 14-day observation period following exposure, all animals appeared active and healthy. There were no signs of gross toxicity, adverse pharmacologic effects, or abnormal behavior.

C. Body Weight - All surviving animals gained body weight over the 14-day observation period.

D. Necropsy - No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

E. Applicant's Conclusions: Under the conditions of this study, the single exposure acute inhalation LC_{50} of SP102000016695 is greater than 2.04 mg/L in male and female rats. Based on the results of this study, SP102000016695 meets the requirements for EPA Toxicity Category IV for inhalation toxicity.

Reviewer: PMRA **Date: July 22, 2008**
Risk Manager (EPA): 25

STUDY TYPE: Primary Eye Irritation - Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL: SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid]

CITATION: Durando, J. (2007) SP102000016695 (636+747+(Inert Ingredient) SC): Primary Eye Irritation Study in Rabbits: (SC 547 Herbicide). Project Number: 21166, P324, M-284730-01-1. Unpublished study prepared by Product Safety Laboratories. 16 p. February 8, 2007. MRID No. 47070313

SPONSOR: Bayer CropScience, 2 T.W. Alexander Drive, P.O. Box 12014, Research Triangle Park, NC 27709

EXECUTIVE SUMMARY: A primary eye irritation test (MRID 47070313) was conducted with rabbits to determine the potential for SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid] to produce irritation from a single instillation via the ocular route. Under the conditions of this study, the test substance is classified as mildly irritating to the eye. Since all ocular irritation cleared by 48 hours of instillation, SP102000016695 meets the requirements for EPA Toxicity Category III for ocular irritation.

One-tenth of a milliliter of the test substance was instilled into the right eye of three healthy rabbits. The left eye remained untreated and served as a control. Ocular irritation was evaluated by the method of Draize *et al.*[1]

Within one hour after test substance instillation, positive conjunctivitis and iritis were noted for all three treated eyes. By 24 hours, corneal opacity developed in one animal. The overall incidence and severity of irritation decreased with time. All animals were free of ocular irritation within 72 hours.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

[1] Draize, J.H., Woodward, G. and Calvery, H.O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. *J. Pharmacol. Exp. Ther.* 1944; 82:377-390.

I. MATERIALS AND METHODS

A. MATERIALS:

1. **Test Material:** SP102000016695
   Description: Light tan opaque liquid
   Lot # 06DAL005P113
   Purity: Thiencarbazone-methyl: 5.81%
   Tembotrione): 29.03%
   CAS #: 317815-83-1; 335104-84-2

2. **Vehicle and/or positive control:** None

3. **Test animals:**

Species:	Rabbit	
Strain:	New Zealand, albino	
Age/weight at dosing:	Young Adult	
Source:	Robinson Services, Inc. Clemmons, NC	
Housing:	Singly housed in suspended stainless steel caging with mesh floors	
Diet:	Purina Rabbit Diet (PMI #5326) *ad libitum*	
Water:	Filtered tap water *ad libitum* by an automatic water dispensing system.	
Environmental conditions:	**Temperature:**	19-21°C
	Humidity:	48-55%RH
	Air changes:	12/hr
	Photoperiod:	12 hrs dark/12 hrs light
Acclimation period:	13 days	

B. STUDY DESIGN and METHODS:

1. **In life dates** - Start: December 5, 2006 End: December 8, 2006

2. **Animal assignment and treatment** - Prior to instillation, two drops of ocular anesthetic (Tetracaine Hydrochloride Ophthalmic Solution, 0.5%) were placed into both the treated and control eye of each animal. One-tenth of a milliliter of the test substance was then instilled into the conjunctival sac of the right eye of each rabbit by pulling the lower lid away from the eyeball. Ocular irritation was evaluated using a high-intensity white light (Mag Lite) in accordance with Draize *et al.* at 1, 24, 48, and 72 hours post-instillation. The fluorescein dye evaluation procedure described in Section 5.A. of the original report was used at 24 hours and as needed at subsequent scoring intervals to evaluate the extent of corneal damage or to verify

reversal of effects. Individual scores were recorded for each animal. In addition to observations of the cornea, iris, and conjunctivae, any other observed lesions were noted.

The animals were observed for signs of gross toxicity and behavioral changes at least once daily during the test period.

II. RESULTS AND DISCUSSION:

A. Within one hour after test substance instillation, positive conjunctivitis and iritis were noted for all three treated eyes. By 24 hours, corneal opacity developed in one animal. The overall incidence and severity of irritation decreased with time. All animals were free of ocular irritation within 72 hours.

The incidence of positive effects, severity and reversibility of irritation are detailed below:

Time Post Instillation	Incidence of Positive Effects		
	Corneal Opacity	Iritis	Conjunctivitis
1 hour	0/3	3/3	3/3
24 hours	1/3	3/3	0/3
48 hours	0/3	0/3	0/3
72 hours	0/3	0/3	0/3

Time Post Instillation	Severity of Irritation – Mean Score
1 hour	13.0
24 hours	10.7
48 hours	0.7
72 hours	0

The Maximum Mean Total Score of SP102000016695 is 13.0.

B. **Applicant's Conclusions:** SP102000016695 is classified as mildly irritating to the eye. Since all ocular irritation cleared by 48 hours of instillation, SP102000016695 meets the requirements for EPA Toxicity Category III for ocular irritation.

Reviewer: PMRA **Date: July 22, 2008**
Risk Manager (EPA): 25

STUDY TYPE: Primary Dermal Irritation - Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid]

CITATION: Durando, J. (2007) SP102000016695 (636+747+(Inert Ingredient) SC): Primary Skin Irritation Study in Rabbits: (SC 547 Herbicide). Project Number: 21167, P326, M-284732-01-1. Unpublished study prepared by Product Safety Laboratories. 16 p. February 8, 2007. MRID No. 47070314

SPONSOR: Bayer CropScience, 2 T.W. Alexander Drive, P.O. Box 12014, Research Triangle Park, NC 27709

EXECUTIVE SUMMARY: A primary skin irritation test (MRID 47070314) was conducted with rabbits to determine the potential for SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid] to produce irritation after a single topical application. Under the conditions of this study, the test substance is classified as slightly irritating to the skin. Since there was slight irritation at 72 hours, SP102000016695, meets the requirements for EPA Toxicity Category IV for dermal irritation.

Five-tenths of a milliliter of the test substance was applied to the skin of three healthy rabbits for 4 hours. Following exposure, dermal irritation was evaluated by the method of Draize *et al.*[1].

There was no edema observed at any treated site during this study. Within one hour of patch removal, all three treated sites exhibited very slight erythema. The overall incidence and severity of irritation decreased with time. All animals were free of dermal irritation by Day 7 (study termination).

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

[1] Draize, J.H., Woodward, G. and Calvery, H.O. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. *J. Pharmacol. Exp. Ther.* 1944; 82:377-390.

I. MATERIALS AND METHODS

A. MATERIALS:

1. **Test Material:** SP102000016695
   Description: Light tan opaque liquid
   Lot # 06DAL005P113
   Purity: Thiencarbazone-methyl: 5.81%
   Tembotrione): 29.03%
   CAS #: 317815-83-1; 335104-84-2

2. **Vehicle and/or positive control:** None

3. **Test animals:**

Species:	Rabbit	
Strain:	New Zealand, albino	
Age/weight at treatment:	Young Adult	
Source:	Robinson Services, Inc. Clemmons, NC	
Housing:	Singly housed in suspended stainless steel caging with mesh floors	
Diet:	Purina Rabbit Diet (PMI #5326) *ad libitum*	
Water:	Filtered tap water *ad libitum* by an automatic water dispensing system.	
Environmental conditions:	**Temperature:**	18-22°C
	Humidity:	54-73%RH
	Air changes:	12/hr
	Photoperiod:	12 hrs dark/12 hrs light
Acclimation period:	8 days	

B. STUDY DESIGN and METHODS:

1. **In life dates** - Start: November 30, 2006 End: December 7, 2006

2. **Animal assignment and treatment** - Animals (3 males) were given a single dose of SP102000016695 dermally using five-tenths of a milliliter applied to one 6-cm^2 intact dose site on each animal and covered with a 1-inch x 1-inch, 4-ply gauze pad. The pad and entire trunk of each animal were then wrapped with semi-occlusive 3-inch Micropore tape to avoid dislocation of the pad. Elizabethan collars were placed on each rabbit and they were returned to their designated cages.

After 4 hours of exposure to the test substance, the pads and collars were removed and the test sites were gently cleansed of any residual test substance.

Individual dose sites were scored according to the Draize scoring system approximately 30-60 minutes, 24, 48, and 72 hours after patch removal. The animals were observed for signs of gross toxicity and behavioral changes at least once daily during the test period.

II. RESULTS AND DISCUSSION:

A. There was no edema observed at any treated site during this study. Within one hour of patch removal, all three treated sites exhibited very slight erythema. The overall incidence and severity of irritation decreased with time. All animals were free of dermal irritation by Day 7 (study termination).

The incidence, severity and reversibility of irritation are detailed below:

	Incidence of Irritation	
Time After Patch Removal	**Erythema**	**Edema**
30-60 minutes	3/3	0/3
24 hours	2/3	0/3
48 hours	2/3	0/3
72 hours	1/3	0/3
Day 7	0/3	0/3

Time After Patch Removal	**Severity of Irritation – Mean Score**
30-60 minutes	1.0
24 hours	0.7
48 hours	0.7
72 hours	0.3
Day 7	0

The Primary Dermal Irritation Index (PDII) calculated for this test substance was 0.7.

B. **Applicant's Conclusions:** SP102000016695 is classified as slightly irritating to the skin. Since there was slight irritation at 72 hours, SP10200001669, meets the requirements for EPA Toxicity Category IV for dermal irritation.

Reviewer: PMRA
Risk Manager (EPA): 25

Date: July 22, 2008

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406, 429

TEST MATERIAL: SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid]

CITATION: Durando, J. (2007) SP102000016695 (636+747+(Inert Ingredient) SC): Dermal Sensitization Study in Guinea Pigs (Buehler Method): (SC 547 Herbicide). Project Number: 21168, P328, M-284733-01-1. Unpublished study prepared by Product Safety Laboratories. 23 p. February 8, 2007. MRID No. 47070315

SPONSOR: Bayer CropScience, 2 T.W. Alexander Drive, P.O. Box 12014, Research Triangle Park, NC 27709

EXECUTIVE SUMMARY: A dermal sensitization test (MRID 47070315) was conducted with guinea pigs to determine the potential for SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid] to produce sensitization after repeated topical applications.

The undiluted test substance was topically applied to twenty healthy test guinea pigs, once each week for a three-week induction period. Twenty-seven days after the first induction dose, a challenge dose of the test substance at its highest non-irritating concentration (HNIC, determined in the preliminary irritation screen to be 100%) was applied to a naive site on each guinea pig. A naive control group (ten animals) was maintained under the same environmental conditions and treated with the test substance at challenge only. Approximately 24 and 48 hours after each induction and challenge dose, the animals were scored for erythema. A table summarizing the incidence and severity of the sensitization response noted after challenge is found below:

	Sensitization Response Indices			
	Incidence of Positive Response[1]		Severity[2]	
	Hours		Hours	
	24	48	24	48
Test Animals	0/20	0/20	0.13	0.05
Naive Control Animals	0/10	0/10	0.15	0.00

Based on the results of this study, SP102000016695is not considered to be a contact sensitizer.

[1] Animals with scores greater than 0.5.
[2] Sum of the erythema scores divided by the number of animals evaluated.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. **Test Material:** SP102000016695
   Description: Light tan opaque liquid
   Lot # 06DAL005P113
   Purity: Thiencarbazone-methyl: 5.81%
   Tembotrione): 29.03%
   CAS #: 317815-83-1; 335104-84-2

2. **Vehicle and/or positive control:** None

3. **Test animals:**

Species:	Guinea Pig	
Strain:	Hartley albino	
Age/weight at start	Young adult	
Source:	Elm Hill Breeding Labs, Chelmsford, MA	
Housing:	Singly housed in suspended stainless steel caging with mesh floors	
Diet:	Pelleted Purina Guinea Pig Chow #5025	
Water:	Filtered tap water *ad libitum* by an automatic water dispensing system.	
Environmental conditions:	**Temperature:**	18-22°C
	Humidity:	52-75%RH
	Air changes/Hour:	11
	Photoperiod:	12 hrs dark/12 hrs light
Acclimation period:	12-19 days	

B. STUDY DESIGN and METHODS:

1. **In life dates** - Start: November 29, 2006 End: December 28, 2006

2. **Animal assignment and treatment** – On the day before initiation, the fur of a group of animals was removed by clipping the dorsal area and flanks. Only healthy animals without pre-existing skin irritation were selected for test. Animals were re-clipped prior to each dose. Once each week for a three week induction phase, four-tenths of a milliliter of the undiluted test substance was shaken well, and then applied to the left side of each test animal using an occlusive 25 mm Hill Top Chamber. The chambers were secured in place and wrapped with

non-allergenic Durapore adhesive tape to avoid dislocation of the chambers and to minimize loss of the test substance. After the 6-hour exposure period, the chambers were removed and the test sites were gently cleansed of any residual test substance. Twenty-seven days after the first induction dose, four-tenths of a milliliter of the undiluted test substance (100%, HNIC) was shaken well, and then applied to a naive site on the right side of each animal as a challenge dose, using the procedures described above. All sites were evaluated for a sensitization response (erythema) approximately 24 and 48 hours after the challenge and induction applications.

In addition to the test animals, 10 guinea pigs (males) from the same shipment were maintained under identical environmental conditions and were treated with the HNIC of the test substance at challenge only. These animals constituted the "naive control" group.

3. Historical positive control validation study: The procedures used in this study were validated using alpha-Hexylcinnamaldehyde Technical (HCA) as a positive control substance. The most recent validation, PSL Study #20608, was performed by Eurofins | Product Safety Laboratories and testing was completed on October 11, 2006. The raw data and report for this study are archived in Eurofins | Product Safety Laboratories Historical Data Notebook No. 03: pages 70, 70A-77. This test was conducted at the Dayton Facility with Hartley strain albino guinea pigs from Elm Hill Breeding Labs following induction and challenge procedures similar to those described above. The results obtained from this testing are presented in Section II. C. below.

II. RESULTS AND DISCUSSION:

A. Induction reactions and duration

Test Animals (100% test substance): Very faint erythema (0.5) was noted for most test sites during the induction phase.

B. Challenge reactions and duration

Test Animals (100% test substance): Very faint erythema (0.5) was noted for five of twenty test sites 24 hours after challenge. Similar irritation persisted at two sites through 48 hours.

Naive Control Animals (100% test substance): Very faint erythema (0.5) was noted for three of ten naive control sites 24 hours after challenge. Irritation was clear from these sites by 48-hours.

A table summarizing the incidence and severity of the sensitization response noted after challenge is found below:

	Sensitization Response Indices			
	Incidence of Positive Response[3]		Severity[4]	
	Hours		Hours	
	24	48	24	48
Test Animals	0/20	0/20	0.13	0.05
Naive Control Animals	0/10	0/10	0.15	0.00

Based on the results of this study, the test substance is not considered to be a contact sensitizer.

C. **Positive control**

Induction Phase

Historical Positive Control Animals (HCA applied undiluted): Very faint to faint erythema (0.5-1) was noted for all positive control sites during the induction phase.

Challenge Phase

Historical Positive Control Animals (75% w/w mixture of HCA in mineral oil): Six of ten positive control animals exhibited signs of a sensitization response (faint erythema [1]) 24 hours after challenge. Similar irritation persisted at three sites through 48 hours. Very faint erythema (0.5) was noted for all other sites after challenge.

Historical Naive Control Animals (75% w/w mixture of HCA in mineral oil): Very faint erythema (0.5) was noted for two of five naive control sites 24 hours after challenge. Irritation persisted at one of these sites through 48 hours.

D. **Applicant's Conclusions:** Based on results of this study, SP102000016695 is not a contact sensitizer. The positive response observed in the historical positive control validation study with alpha-Hexylcinnamaldehyde Technical (HCA) validates the test system used in this study.

[3] Animals with scores greater than 0.5.

[4] Sum of the erythema scores divided by the number of animals evaluated.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D339748
2. **PC CODE:** 015804 & 012801
3. **CURRENT DATE:** 22/JUL/2008
4. **TEST MATERIAL:** SP102000016695 [a formulation containing Thiencarbazone-methyl at 5.81% (certified by analysis) and Tembotrione at 29.03% (certified by analysis); Lot No. 06DAL005P113; light tan opaque liquid]

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity / rat Eurofins/Product Safety Laboratories 21163, P320/UDP, M-284724-01-1 February 8, 2007	47070310	LD_{50} > 2000 mg/kg (females)	III	A
Acute dermal toxicity / rat Eurofins/Product Safety Laboratories 21164, P322/RAT, M-284725-01-1 February 8, 2007	47070311	LD_{50} > 2000 mg/kg (males and females)	III	A
Acute inhalation toxicity / rat Eurofins/Product Safety Laboratories 21165, P330, M-284727-01-1 February 8, 2007	47070312	LC_{50} > 2.04 mg/L (males and females)	IV	A
Primary eye irritation / rabbit Eurofins/Product Safety Laboratories 21166, P324, M-284730-01-1 February 8, 2007	47070313	Corneal opacity in 1/3 eyes & iritis in 3/3 eyes at 24 hrs; resolved by 48	III	A
Primary dermal irritation / rabbit Eurofins/Product Safety Laboratories 21167, P326, M-284732-01-1 February 8, 2007	47070314	Erythema (score 1) in 1 animal at 72 hrs.	IV	A
Dermal sensitization / guinea pig Eurofins/Product Safety Laboratories 21168, P328, M-284733-01-1 February 8, 2007	47070315	Negative	---	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable